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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/627,580	07/28/2000	Timothy W. Woudenberg	4291C3	2453

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EXAMINER	
SHAHNAN SHAH, KHATOL S	
ART UNIT	**PAPER NUMBER**
1645	13

DATE MAILED: 04/09/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

File copy

Office Action Summary	Application No. 09/627,580	Applicant(s) WOUDENBERG ET AL.	
	Examiner Khatol S Shahnan-Shah	Art Unit 1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 December 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 41-58* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 41-58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/2/2002 has been entered.

2. Applicants' amendment D, received 12/2/2002, paper # 12 is acknowledged. New claims 41-58 were added.

Prior Citations of Title 35 Sections

3. The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior office action.

Rejections Withdrawn

4. Rejection of claim 1 under 35 U.S.C. 112, second paragraph, made in paragraph 9 of the office action mailed 5/31/2002, paper # 9 is withdrawn in view of applicants arguments.

5. Rejection of claim 1 under 35 U.S.C. 102 (b) made in paragraph 10 of the office action mailed 5/2/2001, paper # 5 is withdrawn in view of applicants arguments.

New Grounds for Rejection

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are

such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. Claims 1 and 41-58 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fadler et al. (US Patent No. 4,038,151) and further in view of Wu et al. (US 5,612,473) and Bouma et al. (US 5,585,242 and 5,645,801) or Mitsuhashi et al. (US 5,639,612).

The references of Wu et al., Bouma et al. and Mitsuhashi et al. are applied in this rejection because they qualify as prior art under subsection (e) of 35 U.S.C. 102 and accordingly are not disqualified under 35 U.S.C. 103(a).

The claims are drawn to a device for detecting or quantitating a plurality of different polynucleotide sequences (analytes) in a liquid sample comprising a substrate defining a sample distribution net work of (i) sample inlet, (ii) one or more detection chambers and (iii) channel means providing dead end fluid connection.

Fadler et al. disclose an improved device (card) for detecting or quantitating plurality of different analytes in a liquid sample (see column 2, lines 27-29). The device comprises a substrate (rigid plastic plate) with a sample distribution network and one or more detection chambers (wells) (see fig 1 column 1). Each of the wells is connected to a predetermined liquid

specimen supply port by the means of channels, which provide dead-end fluid connection. The device has means to optically read the viewing wells (see column 2, paragraph 6), can be thermoregulated (see column 4, lines 65-66) and uses vacuum system. The device is used for detecting or quantitating " the desired type or types of microorganisms (i.e. plurality of different analytes) in a liquid sample. Fadler et al. differ from the instant invention in failing to teach a device for detecting or quantitating specifically a plurality of polynucleotide sequences, the use of oligonucleotide primers with or without fluorescent labels and of polymerase chain reaction or ligase chain reaction. However, in column 5, lines 34-36 Fadler et al. further teach that: many changes, alterations, modifications and other uses and applications of the subject device will become apparent to those skilled in the art.

Wu et al. teach a rapid and accurate method of detecting multiple polynucleotide analysis in a test sample using a nucleic acid or polynucleotide sequence-based detection system (see column 4, lines 58-61; see column 1, first paragraph, and see column 5, lines 18-20). Wu et al. provide the motivation to use a device, for example such as Fadler's, for accomplishing multiple polynucleotide detection. Wu et al. teach the need in the art for "methods and apparatus for improving the efficiency and decreasing the time required to prepare and amplify multiple targeted nucleic acid sequences within a test sample" and the need for a "simple, user-friendly, cost effective and fast" apparatus. As many as six different target nucleic acid sequences can be amplified and detected thus saving "a tremendous amount of time" (see column 7, first paragraph). Wu et al. discuss the time-consuming and laborious nature associated with the conventional or the prior art detection apparatus, and methods and means of overcoming such problems (see column 9, lines 23-55). Wu et al. further teach the advantages of simultaneous

multiple detection of polynucleotides. Wu et al. teach that such apparatus and methods are "extremely versatile and have broad-reaching applications" such as in "simultaneous detection of ... multiple potentially present microorganisms in biological samples" or in the detection of and "discrimination among multiple potential infectious pathogen" thus permitting rapid diagnosis of infections (see column 7, second and third paragraphs). Wu et al. state that " amplification of multiple analytes potentially present within a sample is generally accomplished by dividing the sample and performing multiple separate PCR amplification procedures using a different primer pair specific for different potential target nucleic acid sequence(s)". Therefore, it would be "advantageous" if multiple analystes such as "multiple target nucleic acid sequences" present in a sample (inclusive of a liquid sample) could be amplified and detected "simultaneously" (see column 15, lines 4-18). The multianalyte recognition is performed with appropriate probe oligonucleicotides (see column 22, lines 47 and 48). The complementary oligonucleotide probes or PCR products labeled with fluorescent dyes or compounds and probes that are exactly or sufficiently complementary to an appropriate region of the target nucleic acid sequences are taught (see the paragraph bridging columns 21 and 22 and the second paragraph in column 22).

The use of different polynucleotide-specific agents in different wells would be obvious to one skilled in the art from Wu's teachings in view of what is already known in the art. For instance, Mitsuhasi et al. clearly disclose the use of plurality of wells or detection chambers in a device immobilized and individually with at least two different polynucleotide-specific detection reagents or primers, which are then contacted with a single sample (see claims 22, 17 and 25). This results in the simultaneous detection of a plurality of polynucleptides in a sample (see

claim 36). The two different polynucleotides probes immobilized individuality to different wells, each being complementary/homologous to nucleotide sequences in polynucleotide analytes specific to different antigens or organisms or a biological component and a second specific primer complementary/homologous to a different sequence. The first and second reagents hybridize to first and second polynucleotide analystes in the same sample. The device and the method simultaneously detect pleural analytes. The detection reagents may be labeled with an enzyme or a fluorescent material and the like (see claims 17-37).

Bouma et al, (US 5,585,242) teach methods of detection of polynucleotides by polymerase chain reaction or ligase chain reaction and methods of detecting multiple target nucleic acid sequences using multiple flourophores specific to each target nucleic acid sequence. Bouma et al. recognize the need in the art for "a method of amplyifing and detecting the target nucleic acid in an operationally simple, yet highly sensitive manner" and in a "closed system" or in a sealed vessel in order to eliminate the potential for contamination (see column 2, paragraphs 4 and 5) and so also the time-consuming and labor intensive prior art detection procedures and problems with the equipment (device) used for sample preparation, preparation of the reaction reagents, amplification and analysis of the reaction products (see column 2, third paragraph).

Bouma et al. (US 5,645,801) teach that the device detection chambers are made of glass or silicon, copper or aluminium (see columns 9 and 13).

It would have been obvious to one skilled in the art at the time the invention was made to apply Fadler's device used for detecting or quantitating a plurality of different microbial analytes for the detection and quantitation, in a liquid sample, of multiple polynucleotides by immobilizing at least two detection chambers or wells with two different polynucleotide-specific

detection reagents as taught by Mitsuhasi et al. and by using Bouma's polymerase chain reaction or ligase chain reaction to produce the instant invention because: (a) There is an identified need in the art for such an user-friendly, device that allows fast, simple, cost-effective and simultaneous detection and discrimination of multiple polynucleotide analytes in a test sample as taught by Wu et al.; (b) There is an art recognized need for a closed device system that allows operationally simple, highly sensitive and contamination-free method of detection of polynucleotides as taught by Bouma etal. And obviously Fadler's device provides such a system; (c) It is economical and advantageous to detect multiple polynucleotide analytes simultaneously in a sample as taught by Wu et al.; (d) Fader et al. teach that their device can be used for other purposes, for detection of multiple polynucleotide analytes, for example, and (e) Mitsuchashi et al. explicitly teach how to accomplish detection of multiple polynucleotides in the same sample by using at least two detection chambers or wells immobilized with two different polynucleotide-specific detection reagents. One skilled in the art would have been motivated to produce the instant invention for the expected benefit of producing a versatile device that avoids time-consuming and labor-intensive procedures and which has broad clinical and diagnostic applications, such as, simultaneous and time saving detection of multiple genetic sequences, or infectious pathogens in biological samples (via polynucleotide detection) thus permitting, for example, rapid diagnosis of infection as taught by Wu et al. A skilled artisan would have had a reasonable expectation of success in using Fadler's device for detection/quantitation of multiple polynucleotide analytes in a liquid sample by using different target-specific primers in different wells as taught by Mitsuhashi in view of what was known in the art at the time of the claimed invention. The invention as a whole would have been obvious to the routineer in a view of the

combined teachings of the references, the contemporary knowledge in the art at the time of invention and the state of the art at the time of the invention.

Conclusion

7. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Khatol Shahnan-Shah whose telephone number is (703) 308-8896. The examiner can normally be reached on 7:30 AM - 4 PM from Monday through Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette F Smith, can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned to is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Khatol Shahnan-Shah, BS, Pharm, MS

Biotechnology Patent Examiner

Art Unit 1645

March 26, 2003

RODNEY P SWARTZ, PH.D
PRIMARY EXAMINER